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Rare atopy in COVID-19 patients or COVID-19 famine in atopic patients?

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Abstract

Background: There are conflicting results in the literature regarding the frequency of allergic diseases in COVID-19 patients. The effect of having an allergic disease on COVID-19 disease severity has been little studied.

Purpose: In this study, we tried to determine the frequency of allergic diseases in COVID-19 patients and the effect of having an allergic disease on COVID-19 disease severity.

Design/Method: A retrospective cross-sectional study was conducted in patients diagnosed with COVID-19 in a state hospital in Istanbul, Turkey. Patients were contacted by phone and those who approved to participate in the study were questioned about their sociodemographic characteristics, body mass index, smoking history, and about their atopic status. Rate of atopic diseases among mild and severe COVID-19 patients and risk estimates for mild disease in atopic and non-atopic COVID-19 patients were calculated.

Results: Study population consisted of 235 adults with COVID-19 (mean age, 45.3 years [standard deviation, 15.0 years]; 139 [59.1%] male). Among study population, 16 (6.8%) subjects had one of the three atopic symptoms, which were wheezing, rhinitis, or eczema. Among the subjects with atopic status, four (1.7%) subjects had wheezing, eight (3.4%) had rhinitis, and four (1.7%) had eczema within the last 12 months. Although atopic status is associated with 3.1 times higher odds for mild disease, being atopic or not being atopic was not found to be associated with COVID-19 severity (P = .054).

Conclusion: The information that atopic diseases are less common in COVID-19 patients may guide clinical risk classification.

KEYWORDS

atopy, COVID-19, eczema, rhinitis, SARS-CoV-2, wheezing

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) epidemic, which started in Wuhan, China, in December 2019 and caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, has completely changed our lives worldwide.[1] It is known that patients with asthma and other allergic diseases are generally more sensitive to influenza viruses such as rhinovirus that cause acute exacerbation.[2,3] In the early stages of the pandemic, it was estimated that the rate of COVID-19, as well as disease mortality and morbidity, would be higher in patients with chronic respiratory disease compared to the healthy population.[4,5] However, the prevalence of asthma and allergic diseases in COVID-19 patients appears to be lower than expected until now.[6-8] These findings support that

asthma cannot be considered as a risk factor for susceptibility to COVID-19 and that there are unexplained missing links in pathogenesis.

In a study conducted in the early stages of the COVID-19 pandemic and involving children and adult patients, it was shown that angiotensin-converting enzyme 2 (ACE2) gene expression in the airways was decreased in patients with asthma and respiratory allergies. The findings of this study potentially explain the low incidence of COVID-19 in patients with asthma and respiratory allergies.[9] Contrary to this information, a national cohort study examining a large number of patients in Korea has evaluated the relationship between allergic diseases and sensitivity to COVID-19 and disease severity. As a result, it was stated that nationwide allergic rhinitis and asthma, especially non-allergic asthma, cause a greater risk of susceptibility to SARS-CoV-2 infection and serious clinical consequences of COVID-19 in Korea.[10] As it is understood, more evidence is needed regarding the relationship between allergic diseases and clinical consequences of COVID-19.

In the present study, we tried to determine the frequency of allergic diseases in COVID-19 patients whose SARS-CoV-2 polymerase chain reaction (PCR) test result was positive. In addition, we tried to determine the effect of having an allergic disease on COVID-19 disease severity.

2 | METHODS

2.1 | Study population and data collection

This retrospective cross-sectional study was conducted in subjects who were diagnosed with COVID-19 based on positive SARS-CoV-2 polymerase chain reaction result in combined nasal-throat swab sample in a state hospital in Istanbul, Turkey. Patients were contacted by phone and those who approved to participate in the study were questioned about their sociodemographic characteristics, body mass index, smoking history, and about their atopic status. The patients were asked, "Have you had wheezing in the last 12 months?" "Have you had a sneezing or runny nose or nasal congestion problem in the last 12 months without a cold or flu?" and "Have you had an itchy rash at any time in the last 12 months?" to assess their atopic status. Subjects earning minimum wage (monthly income approximately less than 355 U.S. dollar) were defined as low income. Study population was grouped according to severity of COVID-19 according to Turkish Ministry of Health COVID-19 guide.[11]

2.2 | Outcomes and measures

Study data were compared between atopic and non-atopic COVID-19 patients. Rate of atopic diseases among mild and severe COVID-19 patients and risk estimates for mild disease in atopic and non-atopic COVID-19 patients were calculated.

2.3 | Statistical analysis

Continuous variables were expressed as mean ± standard deviation (SD) and categorical variables were expressed as numbers (percentages). For comparisons, independent Student's t test and χ^2-test were used for continuous and categorical variables, respectively. Two-by-two contingency tables with odds ratios and 95% confidence intervals were used to assess the association between categorical variables. All statistical tests were two-sided and a P-value < .05 was considered statistically significant. The analyzes were performed using Statistical Package for the Social Sciences® version 22.

2.4 | Standard protocol approvals

The study was approved by Kartal Dr. Lütfi Kırdar Education and Research Hospital Ethics Committee (8 July, 2020—2020/514/181/4).

3 | RESULTS

Study population consists of 235 adults, 139 male, and 96 female, who received diagnosis of COVID-19 in a state hospital in Istanbul, Turkey. Sociodemographic and smoke-related characteristics and severity of COVID-19 of study subjects are summarized in Table 1. Among study population, 16 (6.8%) subjects had one of the three atopic symptoms, which were wheezing, rhinitis, or eczema. Among the subjects with atopic status, four (1.7%) subjects had wheezing, eight (3.4%) had rhinitis, and four (1.7%) had eczema within the last 12 months. Comparison of characteristics of patients with atopic and non-atopic status revealed that mean age and male gender were significantly lower in atopic COVID-19 patients compared to non-atopic COVID-19 patients. Mean body mass index, low income, smoking and severe disease rates were not significantly different between atopic and non-atopic COVID-19 patients (Table 2). Table 3 shows that the risk estimate for mild COVID-19 is high in atopic patients and low in non-atopic patients.

4 | DISCUSSION

In the present study, out of 235 COVID-19 patients, 1.7% had wheezing, 1.7% had eczema, and 3.4% had rhinitis, with atopy rate of only

TABLE 1 Study population characteristics (n = 235)

Age, years (mean ± SD)	45.3 ± 15.0
Male gender	139 (59.1)
Body mass index, kg/m^2 (mean ± SD)	26.3 ± 4.4
Low income	172 (73.2)
Active smoker	33 (14.0)
Severe disease	98 (41.7)

Note: Data are expressed as n (%), unless otherwise stated.
Abbreviation: SD, standard deviation.

TABLE 2 Comparison of characteristics of patients with atopic and non-atopic status (n = 235)

	Atopic patients (n = 16)	Non-atopic patients (n = 219)	*P*
Age, years (mean ± SD)	35.3 ± 10.5	46.0 ± 15.0	.006
Male gender	5 (31.2)	134 (61.2)	.019
Body mass index, kg/m^2 (mean ± SD)	25.5 ± 3.9	26.4 ± 4.4	.452
Low income	9 (56.2)	163 (74.4)	.143
Current smoker	0 (0)	33 (15.1)	.137
Severe disease	3 (18.8)	95 (43.4)	.054

Note: Data are expressed as n (%), unless otherwise stated.

TABLE 3 Risk estimate for mild COVID-19

		95% confidence interval	
	Odds ratio	Lower	Upper
Study population (n = 235)	.301	.083	1.087
Non-atopic patients (n = 219)	.934	.875	.996
Atopic patients (n = 16)	3.100	.908	10.587

6.8%. These rates are much lower than the atopy rate found in previous studies in our country. The prevalence of allergic diseases in Turkey was previously evaluated by a cross-sectional multicenter study. In this study, the frequency of wheezing in people living in urban areas was found between 10.8% and 12%. In the same study, the rates of allergic rhinitis and eczema were found to be 11.7%–17.0% and 6.6%–7.3%, respectively.[12] In a different single-center study in Bolu, Turkey, the prevalence of wheezing was 12.0%, allergic rhinitis was 16.5%, and eczema prevalence was 9.6% in adults aged 30–49 years.[13] In a cross-sectional study conducted in Sivas, Turkey, the rate of wheezing was found to be 20.9%.[14] In these three studies and in our study, the atopy state of the participants was determined by asking them similar questions about atopic symptoms. Therefore, our study has revealed that the rates of atopic diseases in COVID-19 patients are seen to be quite low, looking at previous studies in which the frequency of atopy was evaluated with the same method. The rare occurrence of atopy in patients with COVID-19 can only be explained by the low incidence of COVID-19 disease in atopic individuals or even if they caught COVID-19, the disease is not detected with an asymptomatic course.

The findings of our study support the results of the study conducted in Wuhan, which included the first findings regarding the relationship between allergic diseases and COVID-19. In this study, it was determined that none of the 140 COVID-19 patients followed up in the hospital had asthma, allergic rhinitis, and eczema.[6] Similarly, although the known asthma prevalence in Wuhan was 6.4%, a study evaluating 548 COVID-19 patients in Wuhan, the frequency of asthma was found as low as only 0.9%. In the same study, it was also shown that being asthmatic did not affect the disease severity.[7]

Later the results reported from Europe also supported the initial results in Wuhan, China. The frequency of asthma in COVID-19 patients followed in Brescia and Verona cities of Italy is 1.92% and 1.96%, respectively. However, the actual frequency of asthma reported in the general population in these cities is 6.1% and 6.0%, respectively.[8] And yet, interestingly, none of the asthmatic patients in this study were admitted to the hospital because of an asthma exacerbation due to SARS-CoV-2 infection.[8]

A study published very recently using the electronic medical record database investigated the relationship between atopic diseases and COVID-19 severity. In this study, atopy was found to be associated with significantly lower odds of hospitalization for COVID-19. Also, atopy has been associated with reduced length of stay in hospital for COVID-19. Allergic rhinitis and eczema have been associated with lower hospitalization rates associated with COVID-19. However, contrary to these findings, asthma was associated with increased intubation time. And again, when patients with asthma were grouped into allergic and non-allergic patients, only non-allergic asthma was associated with prolonged intubation time. There was no difference in mortality between groups with or without atopy.[15] In our study, although atopic status is associated with 3.1 times higher odds for mild disease, being atopic or not being atopic was not found to be associated with COVID-19 severity. In a Korean national representative cohort of 219,959 participants testing for SARS-CoV-2 in South Korea, Yang et al investigated the potential association of allergic disorders with the likelihood of SARS-CoV-2 test positivity. They also examined differences in COVID-19 clinical outcomes according to allergic diseases among 7340 patients with confirmed SARS-CoV-2 infection. And contrary to previous findings, in this study, asthma and allergic rhinitis were associated with an increased likelihood of SARS-CoV-2 test positivity and poor clinical results. However, atopic dermatitis was found to be unrelated to the positivity of the SARS-CoV-2 test and the severity of COVID-19.[10]

In conclusion, the relationship between allergic diseases, asthma, and SARS-CoV-2 infection is complex. However, in many studies

including our study, the information that atopic diseases are less common in COVID-19 patients may guide clinical risk classification. This knowledge may be advantageous in future strategies. However, there are studies that found the opposite, and further studies, especially well-planned prospective studies are needed to understand the underlying mechanism of this situation.

The most important limitation of our study is that the evaluation of atopic disease was made on the basis of the questionnaire and confirmatory tests such as pulmonary function tests, total IgE, specific IgE or skin prick tests were not performed. On the other hand, the fact that the rates of atopic diseases in the present study were compared with the rate of atopic disease status in studies conducted with a similar inquiry method partially eliminates this limitation. The most important limitation of our study is that the evaluation of atopic disease was made on the basis of the questionnaire and confirmatory tests such as respiratory function tests, total IgE, specific IgE, or skin prick tests were not performed. On the other hand, the fact that the rates of atopic diseases in the study were compared with the rate of atopic disease status in studies conducted with a similar inquiry method partially eliminates this limitation. Our second limitation is that the study design is retrospective. The clinical significance of the low incidence of atopy in COVID-19 will be revealed by epidemiological studies that will determine the incidence of COVID-19 by following atopic individuals.

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K.A. and T.N. had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. K.A. constructed hypothesis for research. K.A. and T.N. contributed substantially to the study design. Data collection was carried out by T.N. K.A. and T.N. performed data analysis and interpretation. K.A. and T.N. substantially contributed to the writing of the manuscript. K.A. and T.N. approved final manuscript. No funding was received for the study.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

Dr. Aksu reports personal fees from Novartis, personal fees from Astra Zeneca, personal fees from Chiesi, personal fees from Sandoz, personal fees from GlaxoSmithKline, personal fees from İbrahim Etem, personal fees from Abdi İbrahim, outside the submitted work.

Dr. Naziroğlu has nothing to disclose for 3-year period prior to the date of submission.

DATA AVAILABILITY STATEMENT

The dataset used and/or analyzed during the present study is available on reasonable request.

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